

11718476 BIOSIS NO.: 199800500207

Detection of point mutations associated with resistance of

**Helicobacter pylori** to **clarithromycin** by  
**hybridization** in liquid phase.

AUTHOR: Pina Myriam; Occhialini Alessandra; Monteiro Lurdes; Doermann

Henry-Pierre; Megraud Francis(a)

AUTHOR ADDRESS: (a)Lab. Bacteriol., Hop. Pellegrin, Pl. Amelie Raba-Leon,  
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JOURNAL: Journal of Clinical Microbiology 36 (11):p3285-3290 Nov., 1998

ISSN: 0095-1137

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: When the standard procedure for determining **antibiotic** susceptibility of bacteria is used, the results are delayed, especially for bacteria that grow slowly, such as **Helicobacter pylori**. Treatment for this bacterium may involve **clarithromycin**, a compound for which resistance has been associated with point mutations on the 23S **rRNA** gene. This resistance is currently found in organisms isolated from 0 to 15% of patients and jeopardizes the success of the treatment. We have designed a test involving amplification and colorimetric **hybridization** in the liquid phase to detect the mutation at the molecular level. First, four reference strains, including the wild type and three strains with the mutations A2143C, A2143G, and A2144G, were used to optimize the method. Amplification was carried out with primers previously published. The amplified products were added to **probe**-coated microtiter wells. A DNA enzyme immunoassay was used to detect the hybrids. The optimal conditions of the **hybridization** were defined for each **probe**. Nineteen **H. pylori** strains resistant to **clarithromycin** and 22 susceptible according to phenotypic data were submitted to restriction with BsaI and BbsI, and part of the 23S **rRNA** gene was sequenced in order to determine the mutation involved for the resistant strains. The new assay showed a complete correlation with the reference methods, except for one strain. Cross-**hybridizations** as well as application of the reaction to other bacteria did not lead to optical densities higher than the cutoff values chosen with the receiving operating characteristic curve. This method can be easily standardized and gives a result within a day. Its application directly to the biopsy specimens or infected gastric juice is planned in the future.

5/7/11 (Item 11 from file: 5)

DIALOG(R) File 5: Biosis Previews(R)

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11665861 BIOSIS NO.: 199800447592

Molecular mechanisms of **clarithromycin** resistance in

**Helicobacter pylori**.

AUTHOR: Hsieh Pei-Fang; Yang Jhy-Chin; Lin Jaw-Town; Wang Jin-Town(a)

AUTHOR ADDRESS: (a)Graduate Inst. Microbiology, Coll. Med., National Taiwan  
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JOURNAL: Journal of the Formosan Medical Association 97 (7):p445-452 July,  
1998

ISSN: 0929-6646

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Combination **antibiotic** therapy for **Helicobacter pylori** has now become the standard means of treating peptic ulcer diseases. **Clarithromycin** is a newly adopted **antibiotic** for H.

**pylori** eradication. However, resistance to **clarithromycin** reduces the efficacy of **clarithromycin**-containing regimens. We explored mechanisms of **clarithromycin** resistance by evaluating **H. pylori** formacrolide resistance mechanisms reported in **H. pylori** and other bacteria. Degenerate polymerase chain reaction analysis of the **H. pylori** genome failed to yield products homologous to methylase, a drug inactivation enzyme, or efflux pumps. **Clarithromycin** selection in *Escherichia coli* NM522, transformed with an expression library that was constructed with genomic DNA from a **clarithromycin**-resistant strain of **H. pylori**, revealed six clones that conferred **clarithromycin** resistance consistently after retransformation. Southern hybridization and DNA sequencing revealed that four of the six clones contained the same locus. Comparison of DNA and amino acid sequences showed that the 1.3-kb DNA fragment had significant homology to the 3-oxoadipate CoA-transferase subunit A (yxjD) and subunit B (yxjE) of *Bacillus subtilis*. However, the **clarithromycin** inactivation assay and knockout mutation analysis showed that the gene increased **clarithromycin** resistance in *E. coli*, but not in **H. pylori**. In contrast, sequencing of the 23S **rRNA** gene in six **clarithromycin**-resistant **H. pylori** clinical isolates revealed an A to G transitional mutation at position 2515 of the 23S **rRNA** gene in all isolates. Natural transformation with the 23S **rRNA** gene from resistant strains conferred **clarithromycin** resistance in **clarithromycin**-sensitive strains. We conclude that the 23S **rRNA** mutation is sufficient to confer **clarithromycin** resistance and that it is the major mechanism of **clarithromycin** resistance in **H. pylori**.

5/7/12 (Item 12 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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09389976 BIOSIS NO.: 199497398346  
Phylogeny of **Helicobacter** Isolates from Bird and Swine Feces and  
Description of **Helicobacter** pametensis sp. nov.  
AUTHOR: Dewhirst Floyd E(a); Seymour Charles; Fraser Gayle J; Paster Bruce  
J; Fox James G  
AUTHOR ADDRESS: (a)Forsyth Dent. Cent., 140 Fenway, Boston, MA 02115\*\*USA  
JOURNAL: International Journal of Systematic Bacteriology 44 (3):p553-560  
1994  
ISSN: 0020-7713  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Previously, nine fecal isolates from wild birds and a domestic swine were identified as **helicobacters** by phenotypic characterization and reaction with a **helicobacter** genus-specific DNA probe. These isolates fell into three biotypes by analysis of phenotypic traits. To further characterize these isolates, full 16S **rRNA** sequences were determined for strains representing each biotype, and sequence comparison indicated that the strains represented three novel, phylogenetically defined **Helicobacter** species. Three 16S **rRNA**-based DNA probes were designed and used to identify the remaining strains. Probe reactivity divided the strains into the same three groups identified phenotypically. Six of the isolates represented a new species of the genus **Helicobacter** for which we propose the name **Helicobacter** pametensis sp. nov. The following phenotypic features distinguished **H. pametensis** from other **Helicobacter** and **Campylobacter** species: positive tests for oxidase, catalase, alkaline phosphatase, nitrate reduction, growth at 42 degree C, and growth in the presence of 1% glycine; negative tests for urease, gamma glutamyl transpeptidase, indoxyl acetate hydrolysis, and hippurate hydrolysis; and susceptibility

to nalidixic acid and cephalothin. *H. pametensis* cells were motile and possessed one subterminal sheathed flagellum at each end. The two additional **Helicobacter** species were similar to *H. pametensis* except that they were urease positive, hydrolyzed indoxyl acetate, and were resistant to cephalothin. Because these two additional species are phenotypically similar and are represented by only two isolates for one species and one isolate for the other, they are not formally named but are referred to as **Helicobacter** sp. "Bird-B" and **Helicobacter** sp. "Bird-C." These three new **Helicobacter** species can easily be confused with **Campylobacter coli**, **Campylobacter lari**, and **Campylobacter jejuni** if only a limited number of phenotypic traits are used for identification. Since it is now known that birds can harbor **Helicobacter** as well as **Campylobacter** species, methods which clearly distinguish these genera should be used to identify bird **campylobacter**-like isolates or bacterial strains traceable to bird fecal contamination. The zoonotic potential of these new **Helicobacter** species should be examined.

5/7/13 (Item 13 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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08745347 BIOSIS NO.: 199395034698

**Campylobacter helveticus**, new species, a new thermophilic species from domestic animals: Characterization, and cloning of a species-specific DNA probe.

AUTHOR: Stanley John(a); Burnens A P; Linton D; On S L W; Costas M; Owen R J

AUTHOR ADDRESS: (a)National Collection of Type Cultures, Central Public Health Lab., 61 Colindale Ave., London NW9 \*\*UK

JOURNAL: Journal of General Microbiology 138 (11):p2293-2303 1992

ISSN: 0022-1287

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: An atypical group of thermophilic catalase-negative **Campylobacter** strains, the 'CH' (Swiss) group, can be recovered from faeces of domestic cats and dogs after selection by filtration, or with the antibiotic cefoperazone. This group of strains shows no relative DNA homology with any species in **rRNA** superfamily VI (Vandamme et al., 1991, International Journal of Systematic Bacteriology 41, 88-103) except with four thermophilic **Campylobacter** species, notably, *C. upsaliensis*. The group is homogeneous and possess a DNA base composition, cellular morphology at the electron microscope level and phenotypic properties characteristic of **Campylobacter**. Nonetheless it is distinct from known species of **Campylobacter** in terms of conventional bacteriological tests, total cellular protein profile, **rRNA** gene profile, and genomic DNA homology. On the basis of an integrated study of phenotype and genotype, we conclude that these bacteria constitute a previously undescribed species for which we propose the name **Campylobacter helveticus** sp. nov. A species-specific recombinant DNA probe was cloned from the designated type strain (NCTC 12470) for use in identification and further analysis of the epidemiology, pathogenicity and transmission of *C. helveticus*.

5/7/16 (Item 3 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

07561235 Genuine Article#: 181MN Number of References: 21  
Title: Direct detection of **Helicobacter pylori** resistance to

macrolides by a polymerase chain reaction DNA enzyme immunoassay in gastric biopsy specimens  
Author(s): Marais A; Monteiro L; Occhialini A; Pina M; Lamouliatte H; Megraud F (REPRINT)  
Corporate Source: HOP PELLEGRIN, BACTERIOL LAB, PL AMELIE RABA-LEON/F-33076 BORDEAUX//FRANCE/ (REPRINT); HOP PELLEGRIN, BACTERIOL LAB/F-33076 BORDEAUX//FRANCE//; UNIV VICTOR SEGALEN BORDEAUX 2, BACTERIOL LAB/BORDEAUX//FRANCE//; HOP ST ANDRE, SERV MALAD APPAREIL DIGEST/F-33075 BORDEAUX//FRANCE/  
Journal: GUT, 1999, V44, N4 (APR), P463-467  
ISSN: 0017-5749 Publication date: 19990400  
Publisher: BRITISH MED JOURNAL PUBL GROUP, BRITISH MED ASSOC HOUSE, TAVISTOCK SQUARE, LONDON WC1H 9JR, ENGLAND  
Language: English Document Type: ARTICLE  
Abstract: Background-The increasing use of macrolides especially in the treatment of **Helicobacter pylori** infection has led to an increase in resistant strains. The resistance of **H pylori** to macrolides, especially **clarithromycin**, is one of the major causes of eradication failure. In **H pylori**, **clarithromycin** resistance is due to point mutations localised in domain V of 23S **rRNA**.

Aim-To develop a molecular technique based on amplification of a relevant fragment of the 23S **rRNA** and colorimetric **hybridisation** in liquid phase to detect directly in biopsy specimens the type of mutation associated with resistance of **H pylori** to **clarithromycin**.

Methods-Gastric biopsy samples from 61 patients were submitted to this test. The results were compared with standard methods (determination of minimal inhibition concentration, polymerase chain reaction/restriction fragment length polymorphism, and/or DNA sequencing) in order to evaluate the test and to define the cut off values, specificity, and sensitivity.

Results-The 14 biopsy samples in which **H pylori** was not detected did not give a positive result in any assay, and the 14 samples harbouring strains susceptible to **clarithromycin** gave a positive result with the wild type **probe** as expected. The 33 biopsy specimens containing resistant strains always gave a positive signal with one of the probes detecting resistant organisms, but in eight cases they also reacted with the wild type **probe**, indicating that a mixture of resistant and susceptible organisms was present.

Conclusion-The importance of this new assay is that it allows the detection of multiple genotypes corresponding to either heterogeneous genotypes or mixed infections. Moreover, it allows in a single step not only the detection of **H pylori** but also the determination of its susceptibility to **clarithromycin** directly in biopsy specimens without the need for culture.

5/7/17 (Item 4 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

07293368 Genuine Article#: 146WH Number of References: 24  
Title: Microbiological aspects of **antibiotic** resistant **Helicobacter pylori** strains  
Author(s): Monteiro L; Megraud F (REPRINT)  
Corporate Source: CHU BORDEAUX, LAB BACTERIOL ENFANTS, PL AMELIE RABA LEON/F-33076 BORDEAUX//FRANCE/ (REPRINT); PELLEGRIN HOSP, LAB BACTERIOL/BORDEAUX//FRANCE/

Journal: ITALIAN JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, 1998, V30, 3 (OCT), PS329-S333

ISSN: 1125-8055 Publication date: 19981000

Publisher: PACINI EDITORE, VIA DELLA GHERARDESCA-ZONA INDUSTRIALE, 56014 OSPEDALETTO PISA, ITALY

Language: English Document Type: ARTICLE

Abstract: Resistance of **Helicobacter pylori** to antibiotics has been described for macrolides, nitroimidazoles, and fluoroquinolones. In 1996, the mechanism of resistance to macrolides was determined to be a point mutation on the 23S **rRNA** which leads to decreased binding of macrolides to the ribosome. Recently, mutations in the gene coding for nitroreductase have been linked to resistance to nitroimidazoles but more work will be necessary to determine whether this is the only mechanism involved. Point mutations have also been associated with resistance to fluoro-quinolones. A decreased susceptibility to amoxicillin has been observed and may be linked to changes in the penicillin binding proteins. The same phenotypic methods generally used to test **antibiotic** susceptibility can be applied to **Helicobacter pylori**. The disk diffusion method can be used for macrolides, the E-test for amoxicillin, and the point limit method for nitroimidazoles but the reference method of all of these is the agar dilution method. Molecular methods such as polymerase chain reaction E-RFLP and various techniques using **hybridization** can also be employed but to date they have only been used for macrolides. These techniques have the advantage that they can be applied directly to the biopsy specimen.

5/7/18 (Item 5 from file: 34)  
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci  
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05649677 Genuine Article#: WN038 Number of References: 297

Title: Selective detection, enumeration and identification of potentially probiotic Lactobacillus and Bifidobacterium species in mixed bacterial populations

Author(s): Charteris WP (REPRINT) ; Kelly PM; Morelli L; Collins JK

Corporate Source: SET CONSULTANTS LTD, SETCON HOUSE, 43

FRANKFIELD/CORK//IRELAND/ (REPRINT); FOOD RES

ASSOC,/LEATHERHEAD/SURREY/ENGLAND/; NATL DAIRY PROD RES

CTR,/CORK//IRELAND/; UNIV CATTOLICA SACRO CUORE, INST

MICROBIOL/PIACENZO//ITALY/; NATL UNIV IRELAND UNIV COLL CORK, DEPT

MICROBIOL/CORK//IRELAND/

Journal: INTERNATIONAL JOURNAL OF FOOD MICROBIOLOGY, 1997, V35, N1 (MAR 18), P1-27

ISSN: 0168-1605 Publication date: 19970318

Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS

Language: English Document Type: REVIEW

Abstract: Lactobacillus and Bifidobacterium species constitute a significant proportion of probiotic cultures used in developed countries in 'microbial adjunct nutrition'. A number of differential plating methodologies have been developed which seek to selectively detect and enumerate these bacterial groups in bioproducts. Differences in oxygen tolerance, nutritional requirements, **antibiotic** susceptibility, and colony morphology and colour constitute the bases of differentiation in these methods. The choice of methodology depends on the nature of the bioproduct to be examined (wet or dry) and the presence of other bacteria such as starter cultures. In addition, a number of nucleic acid methods have been developed in recent years which enable the specific detection of these bacterial groups at species, subspecies and strain level in mixed populations. The methods use synthetic 16S and 23S **rRNA**-targeted **hybridisation** probes, the specificity of which can be adjusted to fit any taxonomic ranking from genus to genotype, for detection, enumeration and

identification in situ or after differential plating. The combined use of differential plating and molecular strain typing methodologies provides food and medical microbiologists with a powerful and targeted approach to the detection, enumeration and identification of these bacterial groups and their members in a wide range of food and biological materials. An overview of these methods is presented in this review. (C) 1997 Elsevier Science B.V.

5/7/19 (Item 6 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
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05454758 Genuine Article#: WA168 Number of References: 50  
Title: ISOLATION AND MOLECULAR-IDENTIFICATION OF PLANCTOMYCETE BACTERIA  
FROM POSTLARVAE OF THE GIANT TIGER PRAWN, PENAEUS-MONODON  
Author(s): FUERST JA; GWILLIAM HG; LINDSAY M; LICHANSKA A; BELCHER C;  
VICKERS JE; HUGENHOLTZ P  
Corporate Source: UNIV QUEENSLAND, DEPT MICROBIOL/BRISBANE/QLD  
4072/AUSTRALIA/; UNIV QUEENSLAND, CTR MOL & CELLULAR BIOL/BRISBANE/QLD  
4072/AUSTRALIA/; QUEENSLAND UNIV TECHNOL, CTR MOL  
BIOTECHNOL/BRISBANE/QLD 4000/AUSTRALIA/; CSIRO, DIV TROP CROPS &  
PASTURES/ST LUCIA/QLD 4067/AUSTRALIA/; UNIV CALIF BERKELEY, DEPT PLANT &  
MICROBIAL BIOL/BERKELEY//CA/94720  
Journal: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, 1997, V63, N1 (JAN), P  
254-262  
ISSN: 0099-2240  
Language: ENGLISH Document Type: ARTICLE

Abstract: Bacteria phenotypically resembling members of the phylogenetically distinct planctomycete group of the domain Bacteria were isolated from postlarvae of the giant tiger prawn, *Penaeus monodon*. A selective medium designed in the light of planctomycete **antibiotic** resistance characteristics was used for this isolation. Planctomycetes were isolated from both healthy and monodon baculovirus-infected prawn postlarvae. The predominant colony type recovered from postlarvae regardless of viral infection status was nonpigmented. Other, less commonly observed types were pink or orange pigmented. A planctomycete-specific 16S **rRNA**-directed **probe** was designed and used to screen the isolates for their identity as planctomycetes prior to molecular phylogenetic characterization. 16S **rRNA** genes from nine prawn isolates together with two planctomycete reference strains (*Planctomyces brasiliensis* and *Gemmata obscuriglobus*) were sequenced and compared with reference sequences from the planctomycetes and other members of the domain Bacteria. Phylogenetic analyses and sequence signatures of the 16S **rRNA** genes demonstrated that the prawn isolates were members of the planctomycete group. Five representatives of the predominant nonpigmented colony type were members of the *Pirellula* group within the planctomycetes, as were three pink-pigmented colony type representatives. Homology values and tree topology indicated that representatives of the nonpigmented and pink-pigmented colony types formed two discrete clusters within the *Pirellula* group, not identical to any known *Pirellula* species. A sole representative of the orange colony type was a member of the *Planctomyces* group, virtually identical in 16S rDNA sequence to *P. brasiliensis*, and exhibited distinctive morphology.

5/7/20 (Item 7 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

02068013 Genuine Article#: JY118 Number of References: 36  
Title: **CAMPYLOBACTER**-HELVETICUS SP-NOV A NEW THERMOPHILIC SPECIES

FROM DOMESTIC-ANIMALS - CHARACTERIZATION, AND CLONING OF A  
SPECIES-SPECIFIC DNA PROBE

Author(s): STANLEY J; BURNENS AP; LINTON D; ON SLW; COSTAS M; OWEN RJ

Corporate Source: NATL COLLECT TYPE CULTURES, CENT PUBL HLTH LAB, 61

COLINDALE AVE/LONDON NW9 5HT//ENGLAND/; UNIV BERN, INST VET

BACTERIOL, SWISS NATL REFERENCE LAB FOODBORNE DIS/CH-3012

BERN//SWITZERLAND/

Journal: JOURNAL OF GENERAL MICROBIOLOGY, 1992, V138, NOV (NOV), P2293-2303

ISSN: 0022-1287

Language: ENGLISH Document Type: ARTICLE

Abstract: An atypical group of thermophilic catalase-negative

**Campylobacter** strains, the 'CH' (Swiss) group, can be recovered from faeces of domestic cats and dogs after selection by filtration, or with the **antibiotic** cefoperazone. This group of strains shows no relative DNA homology with any species in **rRNA** superfamily VI (Vandamme et al., 1991, International Journal of Systematic Bacteriology 41, 88-103) except with four thermophilic **Campylobacter** species, notably *C. upsaliensis*. The group is homogeneous and possesses a DNA base composition, cellular morphology at the electron microscope level and phenotypic properties characteristic of **Campylobacter**. Nonetheless it is distinct from known species of **Campylobacter** in terms of conventional bacteriological tests, total cellular protein profile, **rRNA** gene profile, and genomic DNA homology. On the basis of an integrated study of phenotype and genotype, we conclude that these bacteria constitute a previously undescribed species for which we propose the name **Campylobacter** helveticus sp. nov. A species-specific recombinant DNA **probe** was cloned from the designated type strain (NCTC 12470) for use in identification and further analysis of the epidemiology, pathogenicity and transmission of *C. helveticus*.

5/7/22 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE

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07486333 EMBASE No: 1998264387

Identification of **Campylobacter** spp by the chemiluminescent **probe**, Accuprobe, Gen-**probe** and susceptibility profile to ciprofloxacin

Houlakis V.; Charvalos E.; Tselentis J.

V. Houlakis, Univ. Regional Hospital of Crete, Bacteriol.,

Parasitol./Zoonoses Lab., Heraklion Crete Greece

Acta Microbiologica Hellenica ( ACTA MICROBIOL. HELL. ) (Greece) 1997, 42/6 (792-795)

CODEN: AMBHA ISSN: 0438-9573

DOCUMENT TYPE: Journal; Article

LANGUAGE: GREEK SUMMARY LANGUAGE: ENGLISH; GREEK

NUMBER OF REFERENCES: 6

Twenty eight **Campylobacter** strains were isolated in the routine laboratory of the University Hospital of Crete during a period of six months and identified as **Campylobacter** spp by the standard biochemical test API Camp, Merieux. The culture confirmation system Gen **probe**, Accuprobe was used for the confirmation of the majority of the strains. The system is based on the use of a chemiluminescent (non radiolabelled) DNA **probe** that is **hybridized** to an **rRNA** target for all **Campylobacter** jejuni, **Campylobacter** coli and **Campylobacter** lari strains. The **probe** does not react to other **Campylobacter** spp. **rRNA** targets. The method is based on the selective chemical degradation of the label. Eighteen strains were **Campylobacter** jejuni and six strains were **Campylobacter** coli, whereas four strains identified by the API Camp as **Campylobacter** fetus did not **hybridize** with the chemiluminescent **probe**; none

of the strains belonged to **Campylobacter lari** spp. The method was proved to be rapid and specific and could provide good discrimination for the most common isolated species in Crete. The efficacy of identification was 100% as compared to the standard biochemical test method. From the twenty eight strains only nine strains showed MICs < 1 ug/ml as tested by the agar dilution method. The majority of the strains (66.6%) were resistant to ciprofloxacin, with MICs > 4 ug/ml. Twelve strains showed MICs > 8 ug/ml. This latest result should be considered with caution as fluoroquinolones are broadly used in human and animals.

5/7/34 (Item 1 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
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136364347 CA: 136(24)364347h JOURNAL  
Rapid and accurate determination of genotypic clarithromycin resistance in cultured *Helicobacter pylori* by fluorescent in situ hybridization  
AUTHOR(S): Russmann, Holger; Adler, Kristin; Haas, Rainer; Gebert, Bettina; Koletzko, Sibylle; Heesemann, Jurgen  
LOCATION: Max von Pettenkofer-Institut fur Hygiene und Medizinische Mikrobiologie, Ludwig Maximilians-Universitat Munchen, Munich, Germany, 80336  
JOURNAL: J. Clin. Microbiol. DATE: 2001 VOLUME: 39 NUMBER: 11 PAGES: 4142-4144 CODEN: JCMIDW ISSN: 0095-1137 LANGUAGE: English PUBLISHER: American Society for Microbiology  
SECTION:  
CA203001 Biochemical Genetics  
CA209XXX Biochemical Methods  
IDENTIFIERS: clarithromycin resistance *Helicobacter* fluorescent situ hybridization  
DESCRIPTORS:  
Antibiotic resistance... DNA... *Helicobacter pylori*...  
comparison of clarithromycin susceptibility testing in cultured *Helicobacter pylori* by fluorescent in situ hybridization, E-test and disk diffusion  
Nucleic acid hybridization...  
in situ, fluorescence; comparison of clarithromycin susceptibility testing in cultured *Helicobacter pylori* by fluorescent in situ hybridization, E-test and disk diffusion  
Drug screening...  
susceptibility testing; comparison of clarithromycin susceptibility testing in cultured *Helicobacter pylori* by fluorescent in situ hybridization, E-test and disk diffusion  
rRNA...  
23 S; comparison of clarithromycin susceptibility testing in cultured *Helicobacter pylori* by fluorescent in situ hybridization, E-test and disk diffusion  
CAS REGISTRY NUMBERS:  
81103-11-9 comparison of clarithromycin susceptibility testing in cultured *Helicobacter pylori* by fluorescent in situ hybridization, E-test and disk diffusion

5/7/35 (Item 2 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
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135353342 CA: 135(25)353342f JOURNAL  
Rapid detection of mutations in the 23S rRNA gene of *Helicobacter pylori* that confers resistance to clarithromycin treatment to the bacterium  
AUTHOR(S): Matsumura, Masayuki; Hikiba, Yoko; Ogura, Keiji; Togo, Goichi; Tsukuda, Izumi; Ushikawa, Kenji; Shiratori, Yasushi; Omata, Masao  
LOCATION: The Institute for Adult Diseases, Asahi Life Foundation, Tokyo,



Japan, 160-0023

JOURNAL: J. Clin. Microbiol. DATE: 2001 VOLUME: 39 NUMBER: 2 PAGES:  
691-695 CODEN: JCMIDW ISSN: 0095-1137 LANGUAGE: English PUBLISHER:  
American Society for Microbiology

SECTION:

CA203001 Biochemical Genetics

CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY

CA214XXX Mammalian Pathological Biochemistry

IDENTIFIERS: Helicobacter 23S rRNA gene point mutation detection

LightCycler PCR, clarithromycin resistant Helicobacter detection

LightCycler PCR

DESCRIPTORS:

Primers(nucleic acid)...

DNA, 23S rRNA gene-specific primers CRFL-1 and CRFL-2; rapid detection  
of mutations in 23S rRNA gene of Helicobacter pylori that confers  
resistance to clarithromycin using LightCycler PCR

PCR(polymerase chain reaction)...

LightCycler, real-time; rapid detection of mutations in 23S rRNA gene  
of Helicobacter pylori that confers resistance to clarithromycin using  
LightCycler PCR

Mutation...

point, A2144G and A2143C; rapid detection of mutations in 23S rRNA gene  
of Helicobacter pylori that confers resistance to clarithromycin which  
is used in treatment of bacterium

DNA...

primer, 23S rRNA gene-specific primers CRFL-1 and CRFL-2; rapid  
detection of mutations in 23S rRNA gene of Helicobacter pylori that  
confers resistance to clarithromycin using LightCycler PCR

Helicobacter pylori... Antibiotic resistance...

rapid detection of mutations in 23S rRNA gene of Helicobacter pylori  
that confers resistance to clarithromycin which is used in treatment of  
bacterium

Probes(nucleic acid)...

23S rRNA gene-specific probes MP-W and AP-2186; rapid detection of  
mutations in 23S rRNA gene of Helicobacter pylori that confers  
resistance to clarithromycin using LightCycler PCR

Gene,microbial...

23S rRNA; rapid detection of mutations in 23S rRNA gene of Helicobacter  
pylori that confers resistance to clarithromycin which is used in  
treatment of bacterium

CAS REGISTRY NUMBERS:

81103-11-9 resistance to; rapid detection of mutations in 23S rRNA gene of  
Helicobacter pylori that confers resistance to clarithromycin which is  
used in treatment of bacterium

372538-52-8 23S rRNA gene-specific primer CRFL-1; rapid detection of  
mutations in 23S rRNA gene of Helicobacter pylori that confers  
resistance to clarithromycin using LightCycler PCR

372538-53-9 23S rRNA gene-specific primer CRFL-2; rapid detection of  
mutations in 23S rRNA gene of Helicobacter pylori that confers  
resistance to clarithromycin using LightCycler PCR

372538-55-1D 3'-labeled with FITC, 23S rRNA gene-specific probe AP-2186;  
rapid detection of mutations in 23S rRNA gene of Helicobacter pylori  
that confers resistance to clarithromycin using LightCycler PCR

372538-54-0D 5'-labeled with LC-Red 640, 23S rRNA gene-specific probe  
MP-W; rapid detection of mutations in 23S rRNA gene of Helicobacter  
pylori that confers resistance to clarithromycin using LightCycler PCR

372538-57-3D 5'-labeled with LC-Red 640, 23S rRNA gene-specific probe  
MP-2143; rapid detection of mutations in 23S rRNA gene of Helicobacter  
pylori that confers resistance to clarithromycin using LightCycler PCR

372538-58-4D 5'-labeled with LC-Red 640, 23S rRNA gene-specific probe  
MP-2144; rapid detection of mutations in 23S rRNA gene of Helicobacter  
pylori that confers resistance to clarithromycin using LightCycler PCR

5/7/36 (Item 3 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
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134247908 CA: 134(18)247908q PATENT

Methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

INVENTOR(AUTHOR): Wilson, David L.; Linz, John E.; Kaneene, John B.; Mansfield, Linda S.; Walker, Robert D.; Newman, Thomas C.

LOCATION: USA

ASSIGNEE: Michigan State University

PATENT: PCT International ; WO 200118017 A1 DATE: 20010315

APPLICATION: WO 2000US24321 (20000905) \*US PV153415 (19990910) \*US PV153417 (19990910) \*US PV210545 (20000609)

PAGES: 88 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07H-021/02A; C07H-021/04B; C12Q-001/68B; C12P-019/34B DESIGNATED COUNTRIES: AE; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

SECTION:

CA203001 Biochemical Genetics

CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY

IDENTIFIERS: *Campylobacter* antibiotic resistance detection PCR

DESCRIPTORS:

Feces...

detection in; methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

Gene,microbial...

flaA; methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

Gene,microbial...

flaB; methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

Gene,microbial...

gyrA; methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

Antibiotic resistance... *Campylobacter jejuni*... Environmental analysis... PCR(polymerase chain reaction)... Primers(nucleic acid)... Probes(nucleic acid)... Test kits...

methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

Gene,microbial...

16S rRNA; methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

CAS REGISTRY NUMBERS:

330488-14-7 nucleotide sequence; methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

330488-20-5 PCR primer JL 223; methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

330488-21-6 PCR primer JL 224; methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

330488-15-8 PCR primer JL 238; methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying antibiotic-resistant strains

330488-16-9 PCR primer JL 239; methods for detecting and enumerating *Campylobacter jejuni* in environmental samples and for identifying

antibiotic-resistant strains  
 330488-17-0 probe TAQ1; methods for detecting and enumerating  
 Campylobacter jejuni in environmental samples and for identifying  
 antibiotic-resistant strains  
 330488-18-1 probe TAQ2; methods for detecting and enumerating  
 Campylobacter jejuni in environmental samples and for identifying  
 antibiotic-resistant strains  
 330488-19-2 probe TAQ3; methods for detecting and enumerating  
 Campylobacter jejuni in environmental samples and for identifying  
 antibiotic-resistant strains  
 85721-33-1 resistance to; methods for detecting and enumerating  
 Campylobacter jejuni in environmental samples and for identifying  
 antibiotic-resistant strains  
 330488-97-6 330488-98-7 330488-99-8 330489-00-4 330489-01-5  
 330489-02-6 330489-03-7 330489-04-8 330689-70-8 unclaimed sequence;  
 methods for detecting and enumerating Campylobacter jejuni in  
 environmental samples and for identifying antibiotic-resistant strains

5/7/37 (Item 4 from file: 399)  
 DIALOG(R)File 399:CA SEARCH(R)  
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132246830 CA: 132(19)246830e JOURNAL  
 Novel method for rapid determination of clarithromycin sensitivity in  
 Helicobacter pylori  
 AUTHOR(S): Gibson, J. R.; Saunders, N. A.; Burke, B.; Owen, R. J.  
 LOCATION: Helicobacter Reference Unit, Laboratory of Enteric Pathogens,  
 Central Public Health Laboratory, London, UK, NW9 5HT  
 JOURNAL: J. Clin. Microbiol. DATE: 1999 VOLUME: 37 NUMBER: 11 PAGES:  
 3746-3748 CODEN: JCMIDW ISSN: 0095-1137 LANGUAGE: English PUBLISHER:  
 American Society for Microbiology  
 SECTION:  
 CA203001 Biochemical Genetics  
 CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY  
 IDENTIFIERS: clarithromycin resistance mutation detection Helicobacter,  
 PCR hybridization Helicobacter macrolide resistance mutation, LightCycler  
 assay Helicobacter clarithromycin sensitivity  
 DESCRIPTORS:  
 Helicobacter pylori...  
 PCR-hybridization assay for detection of clarithromycin  
 resistant-assocd. gene mutations in  
 Antibiotic resistance... Macrolides...  
 PCR-hybridization assay for detection of clarithromycin  
 resistant-assocd. gene mutations in Helicobacter pylori  
 Mutation...  
 point; PCR-hybridization assay for detection of clarithromycin  
 resistant-assocd. gene mutations in Helicobacter pylori  
 Nucleic acid hybridization... PCR(polymerase chain reaction)...  
 rapid detn. of clarithromycin sensitivity in Helicobacter pylori with  
 PCR-hybridization assay  
 Gene,microbial...  
 23 S rRNA; PCR-hybridization assay for detection of clarithromycin  
 resistant-assocd. gene mutations in Helicobacter pylori  
 CAS REGISTRY NUMBERS:  
 81103-11-9 PCR-hybridization assay for detection of clarithromycin  
 resistant-assocd. gene mutations in Helicobacter pylori

5/7/38 (Item 5 from file: 399)  
 DIALOG(R)File 399:CA SEARCH(R)  
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132020800 CA: 132(3)20800h PATENT

Determination of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targeted oligonucleotide probes

INVENTOR(AUTHOR): Haas, Rainer; Trebesius, Karlheinz; Apfel, Heiko

LOCATION: Germany,

ASSIGNEE: Creatogen Biosciences G.m.b.H.

PATENT: PCT International ; WO 9961660 A1 DATE: 19991202

APPLICATION: WO 99EP3527 (19990521) \*DE 19823098 (19980522) \*DE 19916610 (19990413)

PAGES: 84 pp. CODEN: PIXXD2 LANGUAGE: German CLASS: C12Q-001/68A

DESIGNATED COUNTRIES: AE; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM

DESIGNATED REGIONAL: GH; GM; KE; LS; MW; SD; SL; SZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

SECTION:

CA209012 Biochemical Methods

CA203XXX Biochemical Genetics

CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY

CA214XXX Mammalian Pathological Biochemistry

IDENTIFIERS: antibiotic resistance microorganism hybridization mutation specific 23S rRNA target, Helicobacter clarithromycin resistance mutation in situ hybridization probe gastritis

DESCRIPTORS:

Cyclitols... Glycosides...

amino; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targeted oligonucleotide probes

Actinomycetes... Animal tissue... Antibiotic resistance... Bartonella...

Body fluid... Borrelia burgdorferi... Campylobacter coli... Campylobacter

jejuni... Chlamydia... Culture media... Fluorescence microscopy...

Helicobacter felis... Helicobacter fennelliae... Helicobacter heilmannii...

Helicobacter mustelae... Helicobacter pylori... Legionella... Macrolides...

Microorganism... Mycobacterium... Mycoplasma... Nocardia... Porphyromonas

gingivalis... Probes(nucleic acid)... Propionibacterium acnes... Test kits

... Tropheryma whippelii... Wolinella succinogenes...

detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targeted oligonucleotide probes

Stomach,disease...

gastritis; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targeted oligonucleotide probes

Nucleic acid hybridization...

in situ; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targeted oligonucleotide probes

Mutation...

point; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targeted oligonucleotide probes

rRNA...

16 S; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targeted oligonucleotide probes

rRNA...

23 S; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targeted oligonucleotide probes

CAS REGISTRY NUMBERS:

57-92-1 biological studies, detn. of antibiotic resistance of

microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

56-75-7 59-01-8 60-54-8 114-07-8 1403-66-3 1404-04-2 7542-37-2 32385-11-8 32986-56-4 37517-28-5 56391-56-1 80214-83-1 80738-43-8 81103-11-9 83905-01-5 detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251931-90-5 hybridization probe ClaR1 for H.pylori A2058G ClaR, 23S 2051-2067 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251931-91-6 hybridization probe ClaR2 for H.pylori A2059G ClaR, 23S 2051-2067 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251931-92-7 hybridization probe ClaR3 for H.pylori A2058C ClaR, 23S 2051-2067 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251931-93-8 hybridization probe ClaWT for H.pylori wild type ClaR, 23S 2051-2067 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251931-97-2 hybridization probe Hh1 for H.heilmannii, 16S 644-663 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251931-98-3 hybridization probe Hh2 for H.heilmannii, 16S 644-664 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251931-99-4 hybridization probe Hh3 for H.heilmannii, 16S 644-663 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251932-00-0 hybridization probe Hh4 for H.heilmannii, 16S 585-605 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251931-95-0 hybridization probe Hpyl-16S-120b for H.pylori, 16S 120-137 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

125052-14-4 hybridization probe Hpyl-16S-219 for H.pylori, 16S 219-240 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251931-96-1 hybridization probe Hpyl-16S-585 for H.pylori, 16S 585-605 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

251931-94-9 hybridization probe Hpyl-16S-753 for H.pylori, 16S 753-770 region-specific; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

2321-07-5 146397-20-8 probe label; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

128123802 CA: 128(11)123802g PATENT  
 Antisense oligonucleotides as antibacterial agents  
 INVENTOR(AUTHOR): Arrow, Amy; Dale, Roderic M. K.; Thompson, Theresa L.  
 LOCATION: USA  
 ASSIGNEE: Oligos Etc. and Oligos Therapeutics, Inc.  
 PATENT: PCT International ; WO 9803533 A1 DATE: 19980129  
 APPLICATION: WO 97US12961 (19970723) \*US 685575 (19960724)  
 PAGES: 164 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07H-021/00A;  
 A61K-031/70B; C12N-015/11B DESIGNATED COUNTRIES: AL; AM; AU; AZ; BA; BB;  
 BG; BR; BY; CA; CN; CU; CZ; EE; GE; GH; HU; IL; IS; JP; KG; KP; KR; KZ; LC;  
 LK; LR; LT; LV; MD; MG; MK; MN; MX; NO; NZ; PL; RO; RU; SG; SI; SK; SL; TJ;  
 TM; TR; TT; UA; UZ; VN; YU; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM  
 DESIGNATED REGIONAL: GH; KE; LS; MW; SD; SZ; UG; ZW; AT; BE; CH; DE; DK;  
 ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA;  
 GN; ML; MR; NE; SN; TD; TG  
 SECTION:  
 CA201005 Pharmacology  
 CA203XXX Biochemical Genetics  
 CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY  
 IDENTIFIERS: antisense oligonucleotide antibacterial agent  
 DESCRIPTORS:  
 Proteins(specific proteins and subclasses)...  
   antibiotic-binding, antisense oligonucleotides targeted to; antisense  
   oligonucleotides as antibacterial agents  
 Actinomadura... Actinomyces... Aerococcus... Antibacterial agents...  
 Antisense oligonucleotides... Arachnia... Bacillus(bacterium genus)...  
 Bifidobacterium... Clostridium... Corynebacterium... Dermatophilus...  
 Enterococcus... Erysipelothrix... Escherichia coli... Eubacterium...  
 Haemophilus... Helicobacter... Klebsiella... Kurthia... Lactobacillus...  
 Listeria... Micrococcus... Mycobacterium... Neisseria... Nocardia...  
 Nocardiopsis... Nucleic acid hybridization... Pathogenic bacteria...  
 Peptococcus... Peptostreptococcus... Propionibacterium... Pseudomonas...  
 Rhodococcus... Rothia... Salmonella... Serratia... Shigella...  
 Staphylococcus... Streptococcus pneumoniae... Streptococcus pyogenes...  
 Streptococcus... Streptomyces... Vibrio... Yersinia...  
   antisense oligonucleotides as antibacterial agents  
 Periplasm...  
   antisense oligonucleotides targeted to periplasmic proteins; antisense  
   oligonucleotides as antibacterial agents  
 Amino acids,biological studies... Carbohydrates,biological studies... Cell  
 division... Cell wall(microbial)... DNA replication... Fatty  
 acids,biological studies... Lipopolysaccharides... Metabolism(microbial)...  
 mRNA... Outer membrane proteins... Phospholipids,biological studies...  
 Pilus... Ribosomal proteins... rRNA... Secretory proteins... Transport  
 proteins... tRNA... Virulence(microbial)... Vitamins...  
   antisense oligonucleotides targeted to; antisense oligonucleotides as  
   antibacterial agents  
 Nucleic acids...  
   purines and pyrimidines, antisense oligonucleotides targeted to;  
   antisense oligonucleotides as antibacterial agents  
 Proteins(specific proteins and subclasses)...  
   regulatory, antisense oligonucleotides targeted to; antisense  
   oligonucleotides as antibacterial agents  
 CAS REGISTRY NUMBERS:  
 9026-81-7 nuclease-resistant antisense oligonucleotides as antibacterial  
 agents

5/7/40 (Item 7 from file: 399)  
 DIALOG(R) File 399:CA SEARCH(R)  
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126207888 CA: 126(16)207888m JOURNAL  
 A PCR-oligonucleotide ligation assay to determine the prevalence of 23S

rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

AUTHOR(S): Stone, Gregory G.; Shortridge, Dee; Versalovic, James; Beyer, Jill; Flamm, Robert K.; Graham, David Y.; Ghoneim, Adeeb T.; Tanaka, S. Ken

LOCATION: Anti-Infective Res. Div., Abbott Lab., Abbott Park, IL, 60064, USA

JOURNAL: Antimicrob. Agents Chemother. DATE: 1997 VOLUME: 41 NUMBER: 3

PAGES: 712-714 CODEN: AMACCQ ISSN: 0066-4804 LANGUAGE: English

PUBLISHER: American Society for Microbiology

SECTION:

CA203001 Biochemical Genetics

CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY

IDENTIFIERS: clarithromycin resistance *Helicobacter* detection PCR OLA, oligonucleotide ligation assay PCR clarithromycin resistance, rRNA gene PCR OLA clarithromycin resistance, mutation rRNA gene detection clarithromycin resistance

DESCRIPTORS:

PCR(polymerase chain reaction)...

-oligonucleotide ligation assay; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

Genes(microbial)...

for 23S rRNA; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

Antibiotic resistance... *Helicobacter pylori*... Mutation... 23S rRNA...

PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

Genetic methods...

PCR-oligonucleotide ligation assay; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

CAS REGISTRY NUMBERS:

187891-50-5 187891-51-6 amplification primer; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

187891-54-9D biotinylated, A2143C capture probe; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

187891-53-8D biotinylated, A2143G capture probe; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

187891-57-2D biotinylated, A2144C capture probe; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

187891-56-1D biotinylated, A2144G capture probe; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

187891-52-7D biotinylated, wild-type 2143 capture probe; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

187891-55-0D biotinylated, wild-type 2144 capture probe; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

187954-70-7D digoxigenin deriv, 2143 reporter probe; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

187954-69-4D digoxigenin deriv, 2144 reporter probe; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

166839-58-3 mutations of; PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

81103-11-9 PCR-oligonucleotide ligation assay to det. prevalence of 23S rRNA gene mutations in clarithromycin-resistant *Helicobacter pylori*

?

SYSTEM:OS - DIALOG OneSearch

File 5: Biosis Previews(R) 1969-2002/Aug W2  
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\*File 5: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

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\*File 6: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 34: SciSearch(R) Cited Ref Sci 1990-2002/Aug W4  
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\*File 34: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

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(c) 2002 CAB International

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(c) 2002 Internl Academy at Santa Barbara

File 71: ELSEVIER BIOBASE 1994-2002/Aug W3  
(c) 2002 Elsevier Science B.V.

File 73: EMBASE 1974-2002/Aug W3  
(c) 2002 Elsevier Science B.V.

\*File 73: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 76: Life Sciences Collection 1982-2002/Aug  
(c) 2002 Cambridge Sci Abs

File 77: Conference Papers Index 1973-2002/Jul  
(c) 2002 Cambridge Sci Abs

File 94: JICST-EPlus 1985-2002/Jun W5  
(c) 2002 Japan Science and Tech Corp(JST)

\*File 94: There is no data missing. UDs have been adjusted to reflect the current months data. See Help News94 for details.

File 98: General Sci Abs/Full-Text 1984-2002/Jul  
(c) 2002 The HW Wilson Co.

File 103: Energy SciTec 1974-2002/Jul B2  
(c) 2002 Contains copyrighted material

\*File 103: For access restrictions see Help Restrict.

File 143: Biol. & Agric. Index 1983-2002/Jul  
(c) 2002 The HW Wilson Co

File 144: Pascal 1973-2002/Aug W4  
(c) 2002 INIST/CNRS

File 155: MEDLINE(R) 1966-2002/Aug W3

\*File 155: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

File 156: ToxFile 1965-2002/Aug W4  
(c) format only 2002 The Dialog Corporation

\*File 156: This file has been reloaded. Accession Numbers have changed.

File 172: EMBASE Alert 2002/Aug W4  
(c) 2002 Elsevier Science B.V.

File 305: Analytical Abstracts 1980-2002/Aug W2  
(c) 2002 Royal Soc Chemistry

\*File 305: Alert feature enhanced for multiple files, duplicate removal, customized scheduling. See HELP ALERT.

File 369: New Scientist 1994-2002/Jul W4  
(c) 2002 Reed Business Information Ltd.

File 370: Science 1996-1999/Jul W3



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\*File 370: This file is closed (no updates). Use File 47 for more current information.

File 399:CA SEARCH(R) 1967-2002/UD=13708

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Alert feature enhanced for multiple files, etc. See HELP ALERT.

File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

(c) 1998 Inst for Sci Info

Set	Items	Description
---	----	-----
? s	(pylori or helicobacter or campylobacter or heilmanii)	
	117706	PYLORI
	114525	HELICOBACTER
	59868	CAMPYLOBACTER
	63	HEILMANII
S1	168375	(PYLORI OR HELICOBACTER OR CAMPYLOBACTER OR HEILMANII)
? s s1 and rRNA		
	168375	S1
	121832	RRNA
S2	2613	S1 AND RRNA
? s s2 and (antibiotic or clarithromycin)		
	2613	S2
	646468	ANTIBIOTIC
	28420	CLARITHROMYCIN
S3	511	S2 AND (ANTIBIOTIC OR CLARITHROMYCIN)
? s s3 and (hybridi? or probe)		
	511	S3
	810384	HYBRIDI?
	673943	PROBE
S4	98	S3 AND (HYBRIDI? OR PROBE)
? rd s4		
...examined	50 records	(50)
...completed	examining records	
S5	40	RD S4 (unique ite

1783404 BIOSIS NO.: 199900029513

Polymerase chain reaction using 3'-mismatched primers to detected  
**mutation to clarithromycin in Helicobacter pylori**  
clinical isolates.

AUTHOR: Alarcon T; Domingo D; Prieto N; Lopez-Brea M  
AUTHOR ADDRESS: Dep. Microbiol., Hosp. Univ. de la Princesa, Madrid\*\*Spain  
JOURNAL: Gut 43 (SUPPL. 2):pA9-A10 Sept., 1998  
CONFERENCE/MEETING: XIth International Workshop on Gastroduodenal Pathology  
and Helicobacter pylori Budapest, Hungary September 2-5, 1998  
SPONSOR: European helicobacter pylori Study Group  
ISSN: 0017-5749  
RECORD TYPE: Citation  
LANGUAGE: English

8/7/37 (Item 37 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11783397 BIOSIS NO.: 199900029506

Detection of **Helicobacter pylori** 23S rRNA gene  
**mutation** associated with **clarithromycin** resistance using  
preferential homoduplex formation assay (PCR-PHFA).

AUTHOR: Maeda S(a); Yoshida H(a); Ogura K(a); Matsunaga H; Kawamata O;  
Shiratori Y(a); Omata M(a)  
AUTHOR ADDRESS: (a)Univ. Tokyo, Tokyo\*\*Japan  
JOURNAL: Gut 43 (SUPPL. 2):pA7 Sept., 1998  
CONFERENCE/MEETING: XIth International Workshop on Gastroduodenal Pathology  
and Helicobacter pylori Budapest, Hungary September 2-5, 1998  
SPONSOR: European helicobacter pylori Study Group  
ISSN: 0017-5749  
RECORD TYPE: Citation  
LANGUAGE: English

8/7/38 (Item 38 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11725505 BIOSIS NO.: 199800507236

Explaining the bias in the 23S rRNA gene mutations associated with  
**clarithromycin** resistance in clinical isolates of  
**Helicobacter pylori**.

AUTHOR: Debets-Ossenkopp Y J(a); Brinkman A B; Kuipers E J;  
Vandenbroucke-Grauls C M J E; Kusters J G  
AUTHOR ADDRESS: (a)Dep. Clin. Microbiol. Infection Control, Univ. Hosp.  
Vrije Univ., P.O. Box 7057, 1007 MB, Amster\*\*Netherlands  
JOURNAL: Antimicrobial Agents and Chemotherapy 42 (10):p2749-2751 Oct.,  
1998  
ISSN: 0066-4804  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: A single point **mutation** in the 23S rRNA gene of  
**Helicobacter pylori** is known to confer resistance to  
**clarithromycin**. Most prevalent among **clarithromycin**-resistant  
clinical H. **pylori** isolates are the mutations from A-2142 to G and  
A-2143 to G in the 23S rRNA gene. The bias in the 23S rRNA  
gene mutations conferring **clarithromycin** resistance may result from  
the higher MIC, stability of resistance, and growth rate found for the  
strains with the above-mentioned mutations.

8/7/39 (Item 39 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11665970 BIOSIS NO.: 199800447701

**Helicobacter pylori** specific nested PCR assay for the detection of 23S **rRNA** mutation associated with **clarithromycin** resistance.

AUTHOR: Maeda S(a); Yoshida H; Ogura K; Kanai F; Shiratori Y; Omata M  
AUTHOR ADDRESS: (a)Second Dep. Internal Med., Fac. Med., Univ. Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113\*\*Japan  
JOURNAL: Gut 43 (3):p317-321 Sept., 1998  
ISSN: 0017-5749  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Background-**Clarithromycin** is one of the most important antibiotics for **Helicobacter pylori** eradication. However, 5-10% of strains are reported to be resistant. It has been shown that one point mutation in the 23S **rRNA** gene is associated with resistance to **clarithromycin**. Aims-To establish a polymerase chain reaction (PCR) system which amplifies a segment of the 23S **rRNA** gene containing the mutation points with primers specific for **H pylori**, so that **H pylori** infection and the mutation associated with **clarithromycin** resistance can be examined simultaneously. Methods-To detect **H pylori** infection and the mutation simultaneously, primers specific for the **H pylori** 23S **rRNA** gene were designed based on sequence conservation among **H pylori** strains and sequence specificity as compared with other bacteria. DNA from 57 cultured strains and from 39 gastric juice samples was amplified in the seminested 23S **rRNA** PCR. Clinical applicability was evaluated in 85 patients. Results-DNA samples from 57 cultured strains were all amplified. The novel assay and the urease A PCR agreed in 37/39 gastric juice samples with no false positives. The assay did not amplify the DNA of bacteria other than **H pylori**. Eight of 85 samples had the mutation before treatment. In **clarithromycin** based treatment, eradication was achieved in 2/5 (40%) with the mutation and 29/34 (85%) without the mutation. Conclusion-The assay using gastric juice is quick (within 12 hours) and noninvasive (endoscopy not required), enabling rapid initiation of appropriate antibiotic treatment.

8/7/40 (Item 40 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11653397 BIOSIS NO.: 199800435128

Genotypic characterization of **clarithromycin**-resistant and -susceptible **Helicobacter pylori** strains from the same patient demonstrates existence of two unrelated isolates.

AUTHOR: Wang Ge; Jiang Qin; Taylor Diane E(a)  
AUTHOR ADDRESS: (a)Dep. Medical Microbiol. Immunol., Univ. Alberta, Edmonton, AB T6G 2H7\*\*Canada  
JOURNAL: Journal of Clinical Microbiology 36 (9):p2730-2731 Sept., 1998  
ISSN: 0095-1137  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: **Clarithromycin**-susceptible and **clarithromycin**-resistant **Helicobacter pylori** isolates from the same patient were investigated for the mode of development and mechanism of

**clarithromycin** resistance. The **clarithromycin**-resistant strain UA1182 harbors homozygous A-to-G mutations at position 2143 in both copies of the 23S **rRNA** gene and has a phenotype of resistance to **clarithromycin** and clindamycin but no significant resistance to streptogramin B. Pulsed-field gel electrophoresis patterns of NruI- and NotI-digested genomic DNA from the Clas and Clar isolates demonstrated that they are genetically distinct, suggesting that the development of **clarithromycin** resistance is not from the **mutation** of the existing Clas strain but from a completely new strain.

8/7/41 (Item 41 from file: 5)  
DIALOG(R) File 5:Biosis Previews(R)  
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11651076 BIOSIS NO.: 199800432807

Co-detection of **Helicobacter pylori** and of its resistance to **clarithromycin** by PCR.

AUTHOR: Sevin E D Lamarque; Delchier J C; Soussy C J; Tankovic J(a)

AUTHOR ADDRESS: (a)Serv. Bacteriol.-Virol-Hygiene, Hopital Henri Mondor, Creteil\*\*France

JOURNAL: FEMS Microbiology Letters 165 (2):p369-372 Aug. 15, 1998

ISSN: 0378-1097

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Our aim was to develop a rapid molecular test based on polymerase chain reaction-restriction fragment length **polymorphism** (PCR-RFLP) and making it possible to detect **Helicobacter pylori** directly from gastric biopsy samples, and to test its susceptibility to **clarithromycin**. A 629-bp fragment of the 23S **rRNA** gene of **H. pylori** was amplified by PCR and the mutations responsible for **clarithromycin** resistance were detected with BsaI and BbsI restriction endonucleases. Thirty-five gastric samples were tested in parallel by standard microbiologic methods (culture and **clarithromycin** susceptibility testing with E-test strips) and by PCR-RFLP. The 10 culture-negative samples were also PCR-negative. Sixteen out of the 25 culture-positive samples (64%) were PCR-positive. RFLP analysis could be done in 12 cases and the results were in agreement with those of the E-test: susceptibility in five cases, resistance in seven (six A2144G mutations and one A2143G **mutation**).

8/7/42 (Item 42 from file: 5)  
DIALOG(R) File 5:Biosis Previews(R)  
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11619952 BIOSIS NO.: 199800401933

Site-specific mutations in the 23S **rRNA** gene of **Helicobacter pylori** confer two types of resistance to macrolide-lincosamide-streptogramin B antibiotics.

AUTHOR: Wang G E; Taylor Diane E(a)

AUTHOR ADDRESS: (a)Dep. Med. Microbiol. Immunol., Univ. Alberta, Edmonton, AB T6G 2H7\*\*Canada

JOURNAL: Antimicrobial Agents and Chemotherapy 42 (8):p1952-1958 Aug., 1998

ISSN: 0066-4804

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: **Clarithromycin** resistance in **Helicobacter pylori** is mainly due to A-to-G mutations within the

peptidyltransferase region of the 23S **rRNA**. In the present study, cross-resistance to macrolide, lincosamide, and streptogramin B (MLS) antibiotics (MLS phenotypes) has been investigated for several clinical isolates of *H. pylori*. Two major types of MLS resistance were identified and correlated with specific point mutations in the 23S **rRNA** gene. The A2142G **mutation** was linked with high-level cross-resistance to all MLS antibiotics (type I), and the A2143G **mutation** gave rise to an intermediate level of resistance to **clarithromycin** and clindamycin but no resistance to streptogramin B (type II). In addition, streptogramin A and streptogramin B were demonstrated to have a synergistic effect on both MLS-sensitive and MLS-resistant *H. pylori* strains. To further understand the mechanism of MLS resistance in *H. pylori*, we performed in vitro site-directed mutagenesis (substitution of G, C, or T for A at either position 2142 or 2143 of the 23S **rRNA** gene). The site-directed point mutations were introduced into a **clarithromycin**-susceptible strain, *H. pylori* UA802, by natural transformation followed by characterization of their effects on MLS resistance in an isogenic background. Strains with A-to-G and A-to-C mutations at the same position within the 23S **rRNA** gene had similar levels of **clarithromycin** resistance, and this level of resistance was higher than that for strains with the A-to-T **mutation**. Mutations at position 2142 conferred a higher level of **clarithromycin** resistance than mutations at position 2143. All mutations at position 2142 conferred cross-resistance to all MLS antibiotics, which corresponds to the type I MLS phenotype, whereas mutations at position 2143 were associated with a type II MLS phenotype with no resistance to streptogramin B. To explain that A-to-G transitions were predominantly observed in **clarithromycin**-resistant clinical isolates, we propose a possible mechanism by which A-to-G mutations are preferentially produced in *H. pylori*.

8/7/43 (Item 43 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11517589 BIOSIS NO.: 199800298921

High frequency of mutations at position 2144 of the 23S **rRNA** gene in **clarithromycin**-resistant *Helicobacter pylori* strains isolated in Spain.

AUTHOR: Domingo D; Alarcon T; Sanz J C; Sanchez I; Lopez-Brea M

AUTHOR ADDRESS: Dep. Microbiol., Hosp. Universitario de la Princesa, C/Diego de Leon 62, Madrid 28006\*\*Spain

JOURNAL: Journal of Antimicrobial Chemotherapy 41 (5):p573-574 May, 1998

ISSN: 0305-7453

DOCUMENT TYPE: Letter; Article

RECORD TYPE: Citation

LANGUAGE: English

8/7/44 (Item 44 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11503527 BIOSIS NO.: 199800284859

Detection of **clarithromycin** resistance by *Helicobacter pylori* 23S **rRNA** **mutation**: Clinical usage.

AUTHOR: Maeda S; Yoshida H; Ogura K; Ikenoue T; Kanai F; Kato N; Shiratori Y; Omata M

AUTHOR ADDRESS: Univ. Tokyo, Tokyo\*\*Japan

JOURNAL: Gastroenterology 114 (4 PART 2):pA210 April 15, 1998

CONFERENCE/MEETING: Digestive Disease Week and the 99th Annual Meeting of the American Gastroenterological Association New Orleans, Louisiana, USA May 16-22, 1998

SPONSOR: American Gastroenterological Association  
ISSN: 0016-5085  
RECORD TYPE: Citation  
LANGUAGE: English

8/7/45 (Item 45 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11339226 BIOSIS NO.: 199800120558  
Point mutations in the 23S **rRNA** gene of **Helicobacter pylori** associated with different levels of **clarithromycin** resistance.

AUTHOR: Versalovic James(a); Osato Michael S; Spakovsky Klaudia; Dore Maria Pina; Reddy Rita; Stone Gregory G; Shortridge Dee; Flamm Robert K; Tanaka S Ken; Graham David Y

AUTHOR ADDRESS: (a)Dep. Pathol., Mass. Gen. Hosp., Boston, MA 02114\*\*USA  
JOURNAL: Journal of Antimicrobial Chemotherapy 40 (2):p283-286 Aug., 1997  
ISSN: 0305-7453  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Fifty-four of 59 (91.5%) **clarithromycin**-resistant isolates of **Helicobacter pylori** from different patients possessed either the A2143G (formerly A2058G) or the A2144G (formerly A2059G) **mutation** in the gene encoding 23S **rRNA**. The A2143G **mutation** was significantly more likely to occur in isolates with MICs exceeding 64 mg/L (65% versus 30% with the A2144G **mutation**; P = 0.01). The majority (26 of 31; 83.9%) of isolates with the A2143G **mutation** had MICs exceeding 64 mg/L. Peptic ulcer disease recurred in a substantial proportion of patients infected with **H. pylori** strains containing either the A2143G or the A2144G **mutation**.

8/7/46 (Item 46 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11331317 BIOSIS NO.: 199800112649  
Resistance of macrolides in **Helicobacter pylori** and 23S **rRNA** gen point mutations.

AUTHOR: Garcia-Arata M I(a); Baquero F; De Rafael L; Martin De Argila C; Gisbert J P; Boixeda D; Canton R  
AUTHOR ADDRESS: (a)Hosp. Ramon y Cajal, Carretera Colmenar Km 9.1, Madrid 28034\*\*Spain  
JOURNAL: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy 37p58 1997  
CONFERENCE/MEETING: 37th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 28-October 1, 1997  
SPONSOR: ICAAC  
RECORD TYPE: Citation  
LANGUAGE: English

8/7/47 (Item 47 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11265644 BIOSIS NO.: 199800046976  
Macrolide resistance in **Helicobacter pylori**: Rapid detection of point mutations and assays of macrolide binding to ribosomes.  
AUTHOR: Occhialini Alessandra; Urdaci Maria; Doucet-Populaire Florence;

Bebear Cecile Marie; Lamouliatte Herve; Megraud Francis(a)  
AUTHOR ADDRESS: (a)Lab. Bacteriologie, Hopital Pellegrin, Place Amelie  
Raba-Leon, 33076 Bordeaux Cedex\*\*France  
JOURNAL: Antimicrobial Agents and Chemotherapy 41 (12):p2724-2728 Dec.,  
1997  
ISSN: 0066-4804  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Resistance of *Helicobacter pylori* to macrolides is a major cause of failure of eradication therapies. Single base substitutions in the *H. pylori* 23S rRNA genes have been associated with macrolide resistance in the United States. Our goal was to extend this work to European strains, to determine the consequence of this **mutation** on erythromycin binding to *H. pylori* ribosomes, and to find a quick method to detect the **mutation**. Seven pairs of *H. pylori* strains were used, the parent strain being naturally susceptible to macrolides and the second strain having acquired an in vivo resistance during a treatment regimen that included **clarithromycin**. The identity of the strains was confirmed by random amplified polymorphic DNA testing with two different primers, indicating that resistance was the result of the selection of variants of the infecting strain. All resistant strains were found to have point mutations at position 2143 (three cases) or 2144 (four cases) but never on the opposite DNA fragment of domain V of the 23S rRNA gene. The **mutation** was AfwdarwG in all cases except one (AfwdarwC) at position 2143. Using BsaI and BbsI restriction enzymes on the amplified products, we confirmed the mutations of AfwdarwG at positions 2144 and 2143, respectively. Macrolide binding was tested on purified ribosomes isolated from four pairs of strains with (14C)erythromycin. Erythromycin binding increased in a dose-dependent manner for the susceptible strain but not for the resistant one. In conclusion we suggest that the limited disruption of the peptidyltransferase loop conformation, caused by a point **mutation**, reduces drug binding and consequently confers resistance to macrolides. Finally, the macrolide resistance could be detected without sequencing by performing restriction fragment length **polymorphism** with appropriate restriction enzymes.

8/7/48 (Item 48 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11265638 BIOSIS NO.: 199800046970

Cloning and sequence analysis of two copies of a 23S rRNA gene from *Helicobacter pylori* and association of **clarithromycin** resistance with 23S rRNA mutations.

AUTHOR: Taylor Diane E(a); Ge Zhongming; Purych Dale; Lo Tony; Hiratsuka Koji

AUTHOR ADDRESS: (a)Dep. Med. Microbiol. and Immunol., Univ. Alberta, Edmonton, Alberta T6G 2H7\*\*Canada

JOURNAL: Antimicrobial Agents and Chemotherapy 41 (12):p2621-2628 Dec., 1997

ISSN: 0066-4804  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: In this study, two identical copies of a 23S-5S gene cluster, which are separately situated within the *Helicobacter pylori* UA802 chromosome, were cloned and sequenced. Comparison of the DNA sequence of the *H. pylori* 23S rRNA gene with known sequences of other bacterial 23S rRNA genes indicated that the *H.*

*pylori* UA802 23S *rRNA* genes are closely related to those of *Campylobacter* spp. and therefore belong in the proposed Proteobacteria subdivision. The 5'-terminal nucleotide T or A of the 23S *rRNA* is close to a Pribnow box which could be a -10 region of the transcription promoter for the 23S *rRNA* gene, suggesting that a posttranscriptional process is likely not involved in the maturation of the *H. pylori* 23S *rRNA*. Clinical isolates of *H. pylori* resistant to *clarithromycin* were examined by using natural transformation and pulsed-field gel electrophoresis. Cross-resistance to *clarithromycin* and erythromycin, which was transferred by natural transformation from the Clar Eyr donor strain *H. pylori* E to the Clas Erys recipient strain *H. pylori* UA802, was associated with an single A-to-G transition *mutation* at position 2142 of both copies of the 23S *rRNA* in UA802 Clar Eyr mutants. The transformation frequency for Clar and Eyr was found to be approximately  $2 \times 10^{-6}$  transformants per viable cell, and the MICs of both *clarithromycin* and erythromycin for the Clar Eyr mutants were equal to those for the donor isolate. Our results confirmed the previous findings that *mutations* at positions 2142 and 2143 of the *H. pylori* 23S *rRNA* gene are responsible for *clarithromycin* resistance and suggest that acquisition of *clarithromycin* resistance in *H. pylori* could also result from horizontal transfer.

8/7/49 (Item 49 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11244159 BIOSIS NO.: 199800025491  
Prevalence of resistance of *H. pylori* resistance to  
*clarithromycin* and metronidazole following treatment failure and  
genetic basis of resistance to *clarithromycin*.  
AUTHOR: Sevin E(a); Lamarque D; Berrhouma A; Delchier A J C; Soussy C J(a);  
Tankovic J(a)  
AUTHOR ADDRESS: (a)Serv. Bacteriologie-Virologie-Hygiene, Creteil\*\*France  
JOURNAL: Gut 41 (SUPPL. 1):pA10 1997  
CONFERENCE/MEETING: European Helicobacter Pylori Study Group Xth  
International Workshop on Gastroduodenal Pathology and Helicobacter Pylori  
Lisbon, Portugal September 11-14, 1997  
SPONSOR: European Helicobacter pylori Study Group  
ISSN: 0017-5749  
RECORD TYPE: Citation  
LANGUAGE: English

8/7/50 (Item 50 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11244144 BIOSIS NO.: 199800025476  
Preferential A to G *clarithromycin* resistance *mutation* in 23S  
*rRNA* in *Helicobacter pylori* is due to relative higher  
growth rates and MIC of these A to G *mutations*.  
AUTHOR: Debets-Ossenkopp Y J; Brinkman A B; Kuipers E J; Kusters J G;  
Vandenbroucke-Grauls C M J E  
AUTHOR ADDRESS: Vrije Univ., Amsterdam\*\*Netherlands  
JOURNAL: Gut 41 (SUPPL. 1):pA7 1997  
CONFERENCE/MEETING: European Helicobacter Pylori Study Group Xth  
International Workshop on Gastroduodenal Pathology and Helicobacter Pylori  
Lisbon, Portugal September 11-14, 1997  
SPONSOR: European Helicobacter pylori Study Group  
ISSN: 0017-5749  
RECORD TYPE: Citation  
LANGUAGE: English



8/7/51 (Item 51 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11225769 BIOSIS NO.: 199800007101  
Macrolide resistance in **Helicobacter pylori**: Mechanism and stability in strains from **clarithromycin**-treated patients.  
AUTHOR: Hulten Kristina; Gibreel Amara; Skold Ola; Engstrand Lars(a)  
AUTHOR ADDRESS: (a)Swedish Inst. Infect. Dis. Control, S-10521 Stockholm\*\* Sweden  
JOURNAL: Antimicrobial Agents and Chemotherapy 41 (11):p2550-2553 Nov., 1997  
ISSN: 0066-4804  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: **Helicobacter pylori** strains from seven patients treated with **clarithromycin** were investigated for development, mechanism, and stability of resistance. Genetic relatedness between pre- and posttreatment isolates was shown by arbitrary primed PCR. **Clarithromycin** resistance was associated with A-to-G transitions at either position 2143 or 2144 or at both positions 2116 and 2142. In four cases, the mutations were homozygous. The Clar phenotype was stable after 50 subcultivations in vitro. No erythromycin-modifying enzymes or **rRNA** methylases were found by biological assays, PCR and sequencing, or cloning methods.

8/7/52 (Item 52 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10958795 BIOSIS NO.: 199799579940  
Preferential A to G **mutation** in the 23S **rRNA** in **Helicobacter pylori** conferring resistance to **clarithromycin**.  
AUTHOR: Debets-Ossenkopp Y J; Van Der Bijl M W; Kusters J G; Kuipers E J; Vandenbroucke-Grauls C M J E  
AUTHOR ADDRESS: Vrije Univ., Amsterdam\*\*Netherlands  
JOURNAL: Gastroenterology 112 (4 SUPPL.):pA955 1997  
CONFERENCE/MEETING: Digestive Disease Week and the 97th Annual Meeting of the American Gastroenterological Association Washington, D.C., USA May 11-14, 1997  
ISSN: 0016-5085  
RECORD TYPE: Citation  
LANGUAGE: English

8/7/53 (Item 53 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10924088 BIOSIS NO.: 199799545233  
Resistance of **Helicobacter pylori** to antibiotics.  
AUTHOR: Megraud F  
AUTHOR ADDRESS: Lab. de Bacteriol., Enfants, Groupe Hosp. Pellegrin, Place Amelie-Raba-Leon, 33076 Bordeaux Cedex\*\*France  
JOURNAL: Alimentary Pharmacology & Therapeutics 11 (SUPPL. 1):p43-53 1997  
ISSN: 0269-2813  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Resistance of *Helicobacter pylori* to antibiotics included in current regimens used to eradicate *H. pylori* is a major reason for failure. The definition of resistance is not simple, and the clinical relevance of in vitro results must be considered. The different methods of testing antibiotics cannot apply in all cases. Resistance to **clarithromycin** has a low prevalence rate (lt 10%) and its mechanism is well defined (point **mutation** on the 23S **rRNA** genes, and decreased binding of the antibiotics to the ribosome). Its clinical relevance is not questioned and, because of a clear occurrence of a bimodal strain population, the method for detecting resistance is not crucial. Resistance to nitroimidazoles is much more common, probably in the range of 30% or more in Europe. Neither the mechanism of action of metronidazole resistance nor its mechanism of is well known. The redox potential inside the cell which is important in reducing metronidazole to its active metabolite is probably a key element, but the exact metabolites involved are not yet known. Metronidazole resistance was found to be clinically relevant when standard triple therapy was used. The relevance is questioned for triple therapies including a proton pump inhibitor, **clarithromycin** and metronidazole. More clinical data are needed in this field and the use of agar dilutions is recommended to assess the susceptibility of *H. pylori* to metronidazole. The mechanism of resistance to quinolones has been described but these compounds are not currently used for *H. pylori* infection. No resistance has yet been described for amoxycillin but continuous surveillance is needed in order to detect new cases, as was recently the case for tetracycline resistance.

8/7/54 (Item 54 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10898511 BIOSIS NO.: 199799519656  
Evaluation of rapid molecular methods for detection of **clarithromycin** resistance in *Helicobacter pylori*.  
AUTHOR: Szczebara F(a); Dhaenens L; Vincent P; Husson M O  
AUTHOR ADDRESS: (a)Lab. de Bacteriologie-Hygiene, Fac. de Med., 1 place de Verdun, 59045 Lille Cedex\*\*France  
JOURNAL: European Journal of Clinical Microbiology & Infectious Diseases  
16 (2):p162-164 1997  
ISSN: 0934-9723  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Resistance of *Helicobacter pylori* to **clarithromycin** is due to point mutations at position A2143 or A2144 of the *rrnH* 23S **rRNA** gene, each **mutation** creating an additional restriction site for BsaI or MboII. A procedure combining PCR and RFLP analysis was evaluated for detection of these mutations using primers specific for the 23S **rRNA** gene, and BsaI and MboII enzymes. All **clarithromycin**-resistant isolates (8/8), as defined by the MIC, were found to be resistant by PCR-RFLP. No **clarithromycin**-sensitive isolates (14/14) gave a positive reaction.

8/7/55 (Item 55 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10834013 BIOSIS NO.: 199799455158  
A PCR-oligonucleotide ligation assay to determine the prevalence of 23S **rRNA** gene mutations in **clarithromycin**-resistant *Helicobacter pylori*.

AUTHOR: Stone Gregory G(a); Shortridge Dee; Versalovic James; Beyer Jull;  
Flamm Robert K; Graham David Y; Ghoneim Adeeb T; Tanaka S Ken  
AUTHOR ADDRESS: (a)Abbott Lab., Dep. 47T, Build. AP3, 100 Abbott Park Rd.,  
Abbott Park, IL 60064\*\*USA  
JOURNAL: Antimicrobial Agents and Chemotherapy 41 (3):p712-714 1997  
ISSN: 0066-4804  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: We have developed a rapid PCR-oligonucleotide ligation assay that  
can discriminate single base substitutions that are associated with  
**clarithromycin** resistance in **Helicobacter pylori**.  
Susceptible isolates were wild type at positions 2143 and 2144 (cognate  
to 2058 and 2059 in *Escherichia coli*), while 93% of the resistant  
isolates contained A-to-G mutations at either position and 7% of the  
isolates contained A-to-C mutations at position 2143. In addition, the  
MIC for 86% of the resistant isolates with an A2143 **mutation** was  
gtoreq 64 mu-g per ml, and that for 89% of the resistant isolates with an  
A2144 **mutation** was ltoreq 32 mu-g per ml.

8/7/56 (Item 56 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10769631 BIOSIS NO.: 199799390776

23S **rRNA** gene mutations in *H. pylori*: The A2058G **mutation**  
is most prevalent and associated with high level **clarithromycin**  
resistance.

AUTHOR: Versalovic J(a); Osato M(a); Spakovsky K(a); Dore M P(a); Reddy R  
(a); Stone G G; Shortridge D; Flamm R K; Tanaka S K; Graham D Y(a)  
AUTHOR ADDRESS: (a)Baylor Coll. Med., Houston, TX\*\*USA  
JOURNAL: Gut 39 (SUPPL. 2):pA9 1996  
CONFERENCE/MEETING: IXth International Workshop on Gastroduodenal Pathology  
and *Helicobacter pylori* Copenhagen, Denmark October 16-19, 1996  
ISSN: 0017-5749  
RECORD TYPE: Citation  
LANGUAGE: English

8/7/57 (Item 57 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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10513145 BIOSIS NO.: 199699134290

Mechanism of **clarithromycin** resistance in clinical isolates of  
**Helicobacter pylori**.

AUTHOR: Debets-Ossenkopp Y J; Sparrius M; Kusters J G; Kolkman J J;  
Vandenbroucke-Grauls C M J E(a)  
AUTHOR ADDRESS: (a)Dep. Clin. Microbiol. and Infection Control, Univ.  
Hosp., Vrije Univ., P.O. Box 7057, 1007 MB Am\*\*Netherlands  
JOURNAL: FEMS Microbiology Letters 142 (1):p37-42 1996  
ISSN: 0378-1097  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Seventy-three **Helicobacter pylori**-positive patients  
were treated with a combination of **clarithromycin** and ranitidine in  
order to eradicate the bacterium. Eradication was successful in 79.5%. In  
15 patients eradication failed, and in 11 cases this was due to  
**clarithromycin** resistance. In one patient the infecting strain was  
resistant at the onset of treatment, while in the remaining 10 patients  
resistance developed during therapy. These isolates had also become

resistant to various other antibiotics. Random amplified polymorphic DNA and restriction fragment end-labeling analysis of the isolates showed close genetic relatedness between pre- and post-treatment isolates, indicating that resistance was the result of selection of variants of the infecting strain rather than infection with an exogenous resistant strain. Nucleotide sequence comparisons revealed that all resistant isolates had a single base pair **mutation** in the 23S **rRNA**. Since this single point **mutation** results in co-resistance to various antibiotics at high frequencies, caution should be taken when using **clarithromycin** as a single **antibiotic**.

8/7/58 (Item 58 from file: 5)  
DIALOG(R)File 5: Biosis Previews(R)  
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10268741 BIOSIS NO.: 199698723659  
Mutations in 23S **rRNA** are associated with **clarithromycin** resistance in **Helicobacter pylori**.  
AUTHOR: Versalovic James(a); Shortridge Dee; Kibler Kirsten; Griffy Mamie V ; Beyer Jill; Flamm Robert K; Tanaka S Ken; Graham David Y; Go Mae F  
AUTHOR ADDRESS: (a)Div. Digestive Diseases, Dep. Med., Veterans Affairs Med. Cent., 2002 Holcombe Blvd., Houston, T\*\*USA  
JOURNAL: Antimicrobial Agents and Chemotherapy 40 (2):p477-480 1996  
ISSN: 0066-4804  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Twelve **clarithromycin**-resistant **Helicobacter pylori** isolates (100% of resistant isolates examined) from seven different patients each contained an A fwardw G transition **mutation** within a conserved loop of 23S **rRNA**. A fwardw G transition mutations at positions cognate with Escherichia coli 23S **rRNA** positions 2058 and 2059 were identified. **Clarithromycin**-susceptible **H. pylori** isolates from 14 different patients displayed no polymorphisms in a conserved loop within domain V of 23S **rRNA**. The study is the first to report mutations in **H. pylori** associated with resistance to an antimicrobial agent used in established peptic ulcer treatment regimens.

8/7/69 (Item 11 from file: 34)  
DIALOG(R)File 34: SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

06961599 Genuine Article#: 107QN Number of References: 24  
Title: **Antibiotic** resistance in **Helicobacter pylori** infection  
Author(s): Megraud F (REPRINT)  
Corporate Source: HOP PELLEGRIN, BACTERIOL LAB/F-33076 BORDEAUX//FRANCE/ (REPRINT)  
Journal: BRITISH MEDICAL BULLETIN, 1998, V54, N1, P207-216  
ISSN: 0007-1420 Publication date: 19980000  
Publisher: ROYAL SOC MEDICINE PRESS LTD, 1 WIMPOLE STREET, LONDON W1M 8AE, ENGLAND  
Language: English Document Type: ARTICLE  
Abstract: Resistance to antibiotics is considered as the primary reason for failure of eradication therapies, Resistance to **clarithromycin** is due to a decrease in binding to the ribosomes associated with a point **mutation** on the 23S **rRNA**, Its rate in Europe varies from 0-15%, with 5% in the UK. The resistance influences dramatically the success of the treatments, Resistance to metronidazole is due to a lack of reduction of this compound whose genetic basis is still unknown, The

resistance rate in Europe varies from 10-50%, with 25% in the UK, It influences the success of treatments to a lesser extent than **clarithromycin** resistance.

The initial eradication treatment can be prescribed without testing for susceptibility and must include a combination of two antibiotics, while stressing the importance of compliance to the patient, In case of failure, susceptibility testing must be performed.

Few data are currently available on alternative therapeutic strategies when *H. pylori* is resistant to both **clarithromycin** and metronidazole.

8/7/98 (Item 5 from file: 155)  
DIALOG(R) File 155:MEDLINE(R)

09612903 98061120 PMID: 9432314

Identification of a 23S **rRNA** gene mutation in **clarithromycin**-resistant *Helicobacter pylori*.

Stone G G; Shortridge D; Flamm R K; Versalovic J; Beyer J; Idler K; Zulawinski L; Tanaka S K

Anti-infective Research Division, Abbott Laboratories, Abbott Park, IL 60064, USA.

*Helicobacter* (UNITED STATES) Dec 1996, 1 (4) p227-8, ISSN 1083-4389  
Journal Code: 9605411

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

BACKGROUND: Transition mutations (A-G) at residue 2143, cognate to position 2058 in the *Escherichia coli* 23S **rRNA** gene, have been shown to confer resistance to macrolides in *Helicobacter pylori*. This study reports the finding that transversion mutations (A-C) can occur at 2143 as well. MATERIALS AND METHODS: Three **clarithromycin**-resistant *H. pylori* isolated from three different patients after treatment with **clarithromycin** were analyzed for point mutations by cycle sequencing of a 163-bp amplified region surrounding residue 2143 within the conserved loop of the 23S **rRNA** gene. RESULTS: Nucleotide sequence comparisons of a 163-bp amplified product revealed that A-C transversion mutations occurred at position 2143. *H. pylori* isolated from the patients prior to treatment were susceptible to **clarithromycin** and displayed no **polymorphism** at 2143. CONCLUSION: This is the first report to show that A-C transversion mutations at position 2143 can confer resistance to **clarithromycin** in *H. pylori* and further support the role that mutations at position 2143 play in conferring macrolide resistance in *H. pylori*.

Record Date Created: 19980114

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13560033 BIOSIS NO.: 200200188854

Evaluation of a rapid fluorescent in **situ** hybridisation assay for detection of **Helicobacter pylori** and macrolide resistance in gastric biopsy samples.

AUTHOR: Birkner B(a); Trebesius K; Adler K; Harmsen D; Thrippleton I; Haas R

AUTHOR ADDRESS: (a)Gastroenterology Practice, Munich\*\*Germany

JOURNAL: Abstracts of the General Meeting of the American Society for Microbiology 101p261 2001

MEDIUM: print

CONFERENCE/MEETING: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001

ISSN: 1060-2011

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: **H. pylori** causes chronic gastritis, predisposes to gastric and duodenal ulcers, and has been recognised as a gastric carcinogen. Histology of gastric biopsies is currently regarded as the "gold standard" to diagnose **H. pylori** infection. However, no resistance data are obtained by this and many other methods. For phenotypic resistance determination, culture of **H. pylori** is necessary, which is time consuming and often unsuccessful. The development of macrolide resistance is, however, considered as the main reason for failure of **antibiotic** eradication therapy. To overcome this situation we recently developed a fluorescent in **situ** hybridisation (FISH) assay with probes directed against the **rRNA** for the rapid and specific genotypic detection of **H. pylori** and **clarithromycin** resistance in gastric tissue. Consequently, we performed a prospective study with 100 consecutive patients to evaluate the use of FISH. All patients were suffering from dyspepsia and two antrum biopsies were taken from each person. These specimens were sub sampled and analysed in parallel in a blinded manner by a pathologist (modified giemsa stain) and a microbiologist (culture, resistance phenotype by E-test, urease and FISH). According to the European guidelines for clinical trials, patients with at least two positive tests or with a positive culture only were classified as positive (n=32 cases). There was no significant (p=0.05) difference for discordant pairs between histology and FISH (McNemar chi-squared test, matched paired design). The results for resistance testing were in all cases concordant between E-test and FISH. However, in nine cases (28.1%) resistance testing was only possible by FISH. In conclusion, this new molecular method for the laboratory diagnosis of **H. pylori** is at least as reliable as histology with the substantial added value of macrolide resistance testing. FISH may thus, become an invaluable method especially in cases of therapy failures.

10/7/2 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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13547253 BIOSIS NO.: 200200176074

A new approach to detect clarythromycin-resistant **Helicobacter pylori**.

AUTHOR: Wuerttenberger Angela M(a); Barnert Juergen(a); Wagner Theodor; Wienbeck Martin

AUTHOR ADDRESS: (a)III Med Clin, Zentralklinikum, Augsburg\*\*Germany

JOURNAL: Gastroenterology 120 (5 Supplement 1):pA98 April, 2001

MEDIUM: print

CONFERENCE/MEETING: 102nd Annual Meeting of the American Gastroenterological Association and Digestive Disease Week Atlanta, Georgia, USA May 20-23, 2001

ISSN: 0016-5085

RECORD TYPE: Citation  
LANGUAGE: English

10/7/3 (Item 3 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
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13442212 BIOSIS NO.: 200200071033  
Study of mutations in the 23S **rRNA** in **Helicobacter pylori**  
clinical isolates showing intermediate resistance to **clarithromycin**

AUTHOR: Alarcon T(a); Prieto N(a); Domingo D(a); Lopez-Brea M(a)  
AUTHOR ADDRESS: (a) Hosp. de la Princesa, Madrid\*\*Spain  
JOURNAL: IJMM International Journal of Medical Microbiology 291 (Supplement 31):p10-11 September, 2001  
MEDIUM: print  
CONFERENCE/MEETING: 11th International Workshop on Campylobacter, Helicobacter and related Organisms Freiburg, Germany September 01-05, 2001  
ISSN: 1438-4221  
RECORD TYPE: Citation  
LANGUAGE: English

10/7/12 (Item 12 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
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12477181 BIOSIS NO.: 200000230683  
Rapid and specific detection of **Helicobacter pylori** macrolide resistance in gastric tissue by fluorescent in **situ** hybridisation.  
AUTHOR: Trebesius K; Panthel K; Strobel S; Vogt K; Fallner G; Kirchner T; Kist M; Heesemann J; Haas R(a)  
AUTHOR ADDRESS: (a) Max von Pettenkofer Institute for Hygiene and Medical Microbiology, Pettenkoferstr. 9a, D-80336, Munich\*\*Germany  
JOURNAL: Gut 46 (5):p608-614 May, 2000  
ISSN: 0017-5749  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English

ABSTRACT: Background: The development of macrolide resistance in **Helicobacter pylori** is considered an essential reason for failure of **antibiotic** eradication therapies. The predominant mechanism of resistance to macrolides, particularly **clarithromycin**, is based on three defined mutations within 23S **rRNA**, resulting in decreased binding of the **antibiotic** to the bacterial ribosome. Aim: To develop an **rRNA** based whole cell hybridisation method to detect **Helicobacter** species in **situ** within gastric tissue, simultaneously with its **clarithromycin** resistance genotype. Methods: A set of fluorescent labelled oligonucleotide probes was developed, binding either to H **pylori** 16S **rRNA** or 23S **rRNA** sequences containing specific point mutations responsible for **clarithromycin** resistance. After hybridisation and stringent washing procedures, labelling of intact single bacteria was monitored by fluorescence microscopy. The new approach was compared with PCR based assays, histology, and microbiological culture. Results: In comparison with the phenotypic resistance measurement by E test, the genotypic **clarithromycin** resistance correlated perfectly (100%) for 35 H **pylori** isolates analysed. In a set of gastric biopsy specimens (27) H **pylori** infection was confirmed by histology (17/27) and correctly detected by whole cell hybridisation. Five **clarithromycin** resistant

strains were identified in gastric tissue specimens directly. Furthermore, non-cultivable coccoid forms of *H pylori* were easily detectable by whole cell hybridisation. Conclusions: Whole cell hybridisation of *rRNA* holds great promise for cultivation independent, reliable, and rapid (three hours) genotypic determination of *clarithromycin* resistance in *H pylori*. Compared with PCR techniques it is independent of nucleic acid preparations, not prone to inhibition, and allows semi-quantitative visualisation of the bacteria within intact tissue samples.

10/7/14 (Item 1 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2002 Inst for Sci Info. All rts. reserv.

05649677 Genuine Article#: WN038 Number of References: 297  
Title: Selective detection, enumeration and identification of potentially probiotic *Lactobacillus* and *Bifidobacterium* species in mixed bacterial populations  
Author(s): Charteris WP (REPRINT) ; Kelly PM; Morelli L; Collins JK  
Corporate Source: SET CONSULTANTS LTD, SETCON HOUSE, 43 FRANKFIELD/CORK//IRELAND/ (REPRINT); FOOD RES ASSOC,/LEATHERHEAD/SURREY/ENGLAND/; NATL DAIRY PROD RES CTR,/CORK//IRELAND/; UNIV CATTOLICA SACRO CUORE, INST MICROBIOL/PIACENZO//ITALY/; NATL UNIV IRELAND UNIV COLL CORK, DEPT MICROBIOL/CORK//IRELAND/  
Journal: INTERNATIONAL JOURNAL OF FOOD MICROBIOLOGY, 1997, V35, N1 (MAR 18), P1-27  
ISSN: 0168-1605 Publication date: 19970318  
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS  
Language: English Document Type: REVIEW  
Abstract: *Lactobacillus* and *Bifidobacterium* species constitute a significant proportion of probiotic cultures used in developed countries in 'microbial adjunct nutrition'. A number of differential plating methodologies have been developed which seek to selectively detect and enumerate these bacterial groups in bioproducts. Differences in oxygen tolerance, nutritional requirements, **antibiotic** susceptibility, and colony morphology and colour constitute the bases of differentiation in these methods. The choice of methodology depends on the nature of the bioproduct to be examined (wet or dry) and the presence of other bacteria such as starter cultures. In addition, a number of nucleic acid methods have been developed in recent years which enable the specific detection of these bacterial groups at species, subspecies and strain level in mixed populations. The methods use synthetic 16S and 23S *rRNA*-targeted hybridisation probes, the specificity of which can be adjusted to fit any taxonomic ranking from genus to genotype, for detection, enumeration and identification *in situ* or after differential plating. The combined use of differential plating and molecular strain typing methodologies provides food and medical microbiologists with a powerful and targeted approach to the detection, enumeration and identification of these bacterial groups and their members in a wide range of food and biological materials. An overview of these methods is presented in this review.  
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10/7/23 (Item 2 from file: 399)  
DIALOG(R)File 399:CA SEARCH(R)  
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132020800 CA: 132(3)20800h PATENT  
Determination of antibiotic resistance of microorganisms by *in situ* hybridization using mutation-specific 23S *rRNA*-targeted oligonucleotide probes



INVENTOR(AUTHOR): Haas, Rainer; Trebesius, Karlheinz; Apfel, Heiko

LOCATION: Germany,

ASSIGNEE: Creatogen Biosciences G.m.b.H.

PATENT: PCT International ; WO 9961660 A1 DATE: 19991202

APPLICATION: WO 99EP3527 (19990521) \*DE 19823098 (19980522) \*DE 19916610 (19990413)

PAGES: 84 pp. CODEN: PIXXD2 LANGUAGE: German CLASS: C12Q-001/68A

DESIGNATED COUNTRIES: AE; AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZA; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM

DESIGNATED REGIONAL: GH; GM; KE; LS; MW; SD; SL; SZ; UG; ZW; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

SECTION:

CA209012 Biochemical Methods

CA203XXX Biochemical Genetics

CA210XXX MICROBIAL, ALGAL, AND FUNGAL BIOCHEMISTRY

CA214XXX Mammalian Pathological Biochemistry

IDENTIFIERS: antibiotic resistance microorganism hybridization mutation specific 23S rRNA target, Helicobacter clarithromycin resistance mutation in situ hybridization probe gastritis

DESCRIPTORS:

Cyclitols... Glycosides...

amino; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

Actinomycetes... Animal tissue... Antibiotic resistance... Bartonella...

Body fluid... Borrelia burgdorferi... Campylobacter coli... Campylobacter

jejuni... Chlamydia... Culture media... Fluorescence microscopy...

Helicobacter felis... Helicobacter fennelliae... Helicobacter heilmannii...

Helicobacter mustelae... Helicobacter pylori... Legionella... Macrolides...

Microorganism... Mycobacterium... Mycoplasma... Nocardia... Porphyromonas

gingivalis... Probes(nucleic acid)... Propionibacterium acnes... Test kits

... Tropheryma whippelii... Wolinella succinogenes...

detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

Stomach,disease...

gastritis; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

Nucleic acid hybridization...

in situ; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

Mutation...

point; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

rRNA...

16 S; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

rRNA...

23 S; detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

CAS REGISTRY NUMBERS:

57-92-1 biological studies, detn. of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes

56-75-7 59-01-8 60-54-8 114-07-8 1403-66-3 1404-04-2 7542-37-2

32385-11-8 32986-56-4 37517-28-5 56391-56-1 80214-83-1 80738-43-8  
 81103-11-9 83905-01-5 detn. of antibiotic resistance of  
 microorganisms by in situ hybridization using mutation-specific 23S  
 rRNA-targetted oligonucleotide probes

251931-90-5 hybridization probe ClaR1 for H.pylori A2058G ClaR, 23S  
 2051-2067 region-specific; detn. of antibiotic resistance of  
 microorganisms by in situ hybridization using mutation-specific 23S  
 rRNA-targetted oligonucleotide probes

251931-91-6 hybridization probe ClaR2 for H.pylori A2059G ClaR, 23S  
 2051-2067 region-specific; detn. of antibiotic resistance of  
 microorganisms by in situ hybridization using mutation-specific 23S  
 rRNA-targetted oligonucleotide probes

251931-92-7 hybridization probe ClaR3 for H.pylori A2058C ClaR, 23S  
 2051-2067 region-specific; detn. of antibiotic resistance of  
 microorganisms by in situ hybridization using mutation-specific 23S  
 rRNA-targetted oligonucleotide probes

251931-93-8 hybridization probe ClaWT for H.pylori wild type ClaR, 23S  
 2051-2067 region-specific; detn. of antibiotic resistance of  
 microorganisms by in situ hybridization using mutation-specific 23S  
 rRNA-targetted oligonucleotide probes

251931-97-2 hybridization probe Hh1 for H.heilmannii, 16S 644-663  
 region-specific; detn. of antibiotic resistance of microorganisms by in  
 situ hybridization using mutation-specific 23S rRNA-targetted  
 oligonucleotide probes

251931-98-3 hybridization probe Hh2 for H.heilmannii, 16S 644-664  
 region-specific; detn. of antibiotic resistance of microorganisms by in  
 situ hybridization using mutation-specific 23S rRNA-targetted  
 oligonucleotide probes

251931-99-4 hybridization probe Hh3 for H.heilmannii, 16S 644-663  
 region-specific; detn. of antibiotic resistance of microorganisms by in  
 situ hybridization using mutation-specific 23S rRNA-targetted  
 oligonucleotide probes

251932-00-0 hybridization probe Hh4 for H.heilmannii, 16S 585-605  
 region-specific; detn. of antibiotic resistance of microorganisms by in  
 situ hybridization using mutation-specific 23S rRNA-targetted  
 oligonucleotide probes

251931-95-0 hybridization probe Hpyl-16S-120b for H.pylori, 16S 120-137  
 region-specific; detn. of antibiotic resistance of microorganisms by in  
 situ hybridization using mutation-specific 23S rRNA-targetted  
 oligonucleotide probes

125052-14-4 hybridization probe Hpyl-16S-219 for H.pylori, 16S 219-240  
 region-specific; detn. of antibiotic resistance of microorganisms by in  
 situ hybridization using mutation-specific 23S rRNA-targetted  
 oligonucleotide probes

251931-96-1 hybridization probe Hpyl-16S-585 for H.pylori, 16S 585-605  
 region-specific; detn. of antibiotic resistance of microorganisms by in  
 situ hybridization using mutation-specific 23S rRNA-targetted  
 oligonucleotide probes

251931-94-9 hybridization probe Hpyl-16S-753 for H.pylori, 16S 753-770  
 region-specific; detn. of antibiotic resistance of microorganisms by in  
 situ hybridization using mutation-specific 23S rRNA-targetted  
 oligonucleotide probes

2321-07-5 146397-20-8 probe label; detn. of antibiotic resistance of  
 microorganisms by in situ hybridization using mutation-specific 23S  
 rRNA-targetted oligonucleotide probes